Submission for Docket No. CDC-2020-0029
Agency: Centers for Disease Control and Prevention (HHS)

Stefan G. Kertesz, MD, MSc
Ajay Manhapra, MD
Adam J. Gordon, MD, MPH

June 15, 2020

We offer these comments in response to Docket No. CDC-2020-0029, with the goal of assisting "*CDC's understanding of stakeholders' values and preferences regarding pain management and will complement CDC's ongoing work assessing the need for updating or expanding the CDC Guideline for Prescribing Opioids for Chronic Pain*."

This letter will make 3 points. They are:

I. **Severe chronic pain is a complex human condition, considered by many a disease in its own right.[1] The most authoritative scientific framework for study of chronic pain should play a role in devising recommendations for pain care. That framework was offered by the International Association for the Study of Pain in 2015, and the CDC should embrace it going forward, or it risks endorsing reductionistic and distortive approaches to care.**

II. **The 2016 CDC Guideline's emphasis on a dose threshold of 90 Morphine Milligram Equivalents (MME) does not adequately capture a contemporary understanding of overdose risk in persons who receive prescribed opioids. While the Guideline was laudable in many aspects, the emphasis on MME and the subsequent interpretation of MME targets, should be corrected.**

III. **The 2016 CDC Guideline did not adequately consider the context in which its authority would be invoked. A wide range of federal and non-federal agencies, including law enforcement and quality metric agencies, have enshrined the CDC's 90 MME threshold in ways that traumatize patients. Because this is taking place across many agencies, including US Department of Health and Human Services, the CDC must evaluate the use and misuse of its Guideline more robustly, and remediate through appropriate action.**

After reviewing our qualifications, we cover the three topics where we believe there were, in retrospect, shortfalls in the 2016 CDC Guideline on Prescribing Opioids for Chronic Pain.[2] These shortfalls opened the door for unintended misuse of the Guideline in ways that caused serious harm to many patients and their families. Credible efforts by the CDC to mitigate those harms, beginning in 2019,[2] failed to gain traction with payers, quality metric agencies, state regulators or other agencies within the US Department of Health and Human Services, as we will review. The net result is ongoing risk and harm to a vulnerable contingent of patients. If the CDC wishes to further influence care of long-term pain, it will have to address these shortfalls. With the publication of any future guideline, the CDC should affirm that it has the obligation to evaluate and to remediate inappropriate interpretations or actions that reference its recommendations.

Qualifications. All three of us are front-line clinician-scholars who care for patients with severe long-term pain, opioid use disorder, medical morbidity and social vulnerability. We are internal medicine physicians with certification in addiction medicine, holding joint positions in the Department of Veterans Affairs, Veterans Health Administration (VA) and non-VA academic institutions. Dr. Kertesz has focused a 24-year career on optimizing care delivery to high-vulnerability populations, with research funding from the National Institute on Drug Abuse and the VA Health Services Research & Development branch. He serves on three opioid-related teams at Birmingham VA Medical Center and has published extensively on opioid safety and problems faced by patients with long-term pain, ultimately helping to spur declarations by the CDC itself, and policy adjustments by CMS in 2018. Dr. Manhapra leads the High-Risk Pain Patient Aligned Care Team at VA Hampton Health Care System. He has published and taught about complex chronic pain as an expression of multi-morbidity.[3] His account of problems related to opioid taper in the context of dependence[4] is central to the HHS Guidance on dose reduction issued in 2019.[5] Dr. Gordon is a Professor of Medicine and Psychiatry at the University of Utah and Chief of Addiction Medicine at the VA Salt Lake City Health Care System. He serves as Editor in Chief for the scholarly journal, Substance Abuse and has authored over 220 peer-reviewed papers, mostly on care for populations with pain, addiction and overdose risk. He has been a grantee on dozens of federal grants. He also has been a member of Guideline development teams and authored guidelines for many organizations, including the VA, the Substance Abuse Mental Health Services Administration, and the American Society of Addiction Medicine.

We affirm that we do not speak on behalf of VA, the federal government, our affiliated universities, or any other institution or organization. The opinions that follow are our own.

In this letter we lay out three areas of concern that merit the CDC's attention should it attempt to modify or rewrite its 2016 Guideline, or to reconsider its role in guiding pain care more broadly.

I. Severe chronic pain is a complex human condition, considered by many a disease in its own right. The most authoritative scientific framework for study of chronic pain should play a role in devising recommendations for pain care. That framework was offered by the International Association for the Study of Pain in 2015, and the CDC should embrace it going forward, or it risks endorsing reductionistic and distortive approaches to care.

Optimal care for patients with severe chronic pain should be guided by appropriate assessment and therapeutic decisions rooted in a diagnostic and functional evaluation. The authoritative frameworks for considering pain diagnosis[6] and functional impact,[7] are those offered by the International Association for the Study of Pain in 2015.[8] However, these frameworks are absent from reviews of pain therapies commissioned by AHRQ,[9-11] absent from the CDC's Guideline of 2016,[12] and absent from other leading guidelines focused on opioids.[13,14]

This mismatch between pain science and pain guidance may have been unavoidable in retrospect. However, it made the widely recognized misapplication of opioid guidelines[2,15-17] inevitable. As we will explain, it's impossible to apply an "opioid guideline" when the complexity of the clinical condition being managed (chronic pain), and the components of sound clinical decision-making, are barely acknowledged in the guideline itself.

Federal data estimate 50 million adults have chronic pain and 19.6 million have pain that limits life or work activities on most days.[18] Chronic pain is associated with a range of serious medical illnesses, psychological comorbidities, environmental, and demographic factors.[19] While pain

may manifest based on a physical stimulus, it is clear that these associated factors contribute to pain severity and, reciprocally, some of these factors are aggravated by pain.

The International Association for the Study of Pain (IASP) determined that historic pain classifications (like ICD-10) either failed to represent chronic pain's diversity, or did so poorly.[6] To address that, the IASP proposed a 7-category diagnostic classification, including one primary pain category, and six other categories where chronic pain is secondary (e.g. chronic cancer-related pain, chronic post-surgical pain).[6] IASP's workgroup on functional assessment further asserts that care must incorporate functional assessments related to daily activities, social circumstances, and environmental factors that promote better or worse outcomes.[7] The IASP justifies this point of emphasis because "people with one and the same clinical condition can vary substantially in terms of disability."[7] All of these factors matter for care, but received minimal discussion the 2016 Guideline.

To put it a different way, the pain experience is complex, heterogeneous, dependent on life history, life functioning, family support, comorbid medical illness, psychological conditions, and even prior harms from health providers. Care decisions, including the decision whether or not to offer opioids or other forms of intervention, should be individualized to incorporate:[20]

- Research evidence
- Patient's clinical state
- Patient's preferences
- Clinical context

The CDC's 2016 Guideline, like others issued at the time, did not lay this out. And for this reason, we have a concern that new evidence summaries commissioned by the Agency for Healthcare Research and Quality (AHRQ) to guide federal policy (on opioids,[9] non-opioid pharmacologic pain therapies,[10] and non-pharmacologic therapies[11]) are not as helpful as they could be. This is not because they are invalid or inaccurate. Rather, the reviews reflect layers of simplification built into the source trials, and further reductions of data that are natural to an evidence summation, but that prove distortive in guiding clinical decisions.

To be clear, the AHRQ reviews declare an actuality: across trials, there are only modest mean benefits for opioids, and for some other treatments, across wide ranges of patients, and contexts. The math of averages suggests that there is no treatment that will help most patients greatly, and that some treatments will benefit some patients, to varying degrees. An emphasis on averages routinely invites sweeping declarations that "opioids are no better" than anything else, and often is taken to imply that their use is itself misguided.

But the "actuality" in the three AHRQ reports does not encompass the "reality" that IASP has urged be assessed in care of patients, or the reality that "research evidence" (however limited) is but one of four components clinicians need to consider when making the right clinical decision for a given patient.

For this reason we urge the CDC to approach its work in a way that acknowledges the problems with drafting guidance on pain care if the guidance itself is based on a reductive comparison of treatment effect means that **obscures most of what clinicians, patients and families and the IASP urge be considered**.

This gap becomes more fraught when prescription of opioids enters the discussion. As we have written, there has been appropriate concern and correction regarding overuse of prescription opioids.[16,21] That spurred quality metrics and legal standards that attempt to manage opioid prescribing in isolation from other aspects of pain care,[22] which has caused problems laid out in section III.

II. The 2016 CDC Guideline's emphasis on a dose threshold of 90 Morphine Milligram Equivalents (MME) does not adequately capture a contemporary understanding of overdose risk in persons who receive prescribed opioids. While the Guideline was laudable in many aspects, the emphasis on MME and the subsequent interpretation of MME targets, should be corrected.

The CDC's emphasis on the 90 MME threshold for opioid prescriptions did not represent the best point of leverage to reduce opioid overdose risk at the time the 2016 CDC Guideline was issued. The sources cited by the CDC in 2016, to be sure, reflected valid retrospective analyses,[23-25] and we deduce that a higher prescribed opioid dose (MME per day) incurs greater risk for opioid-related harm.[23,25-27] **However, to date, there is no sound literature to show that reduction in prescribed dose confers any reduction in the risk of opioid-related harm.**

Further, as we discuss, the emphasis on dose threshold as the primary point of leverage for protecting patients was not entirely respectful of the pre-2016 literature, or literature that has followed. That research more strongly supports a view that, in patients receiving opioids by prescription, overdose events emerge from a constellation of risks, including instability of the patient's life, instability in the care relationships, and instability of the dose itself. Forced dose reductions, a course of action reinforced by health systems and the current clinical environment, exacerbate that instability.[28] The literature summarized below shows that clinical risk, in prescription-receiving patients is only partly related to prescription dose, and that clinical risk can rise after opioid stoppage.

a) In historic studies of heroin overdose, **most decedents had low serum morphine levels,** but had coexisting medical illness and had used heroin in unfamiliar circumstances, suggesting "life instability" as a key risk,[29] as opposed to quantified heroin dose.

b) In a retrospective study of overdoses by Bohnert et al, mental illness, younger age and white race were all associated with overdose risk, in addition to prescribed dose.[24] The seeming "protective effect" of age 60-69 years (versus 20-29) was profound (OR 0.2, 95% CI 0.08-0.40). Because age is **not** a plausible protector against drug toxicity, this hints that there were unmeasured factors important to overdose risk. **The CDC Guideline's focus on prescription dose encouraged a misdirection of effort** toward forced dose reduction in older patients who were on higher doses, and away from protecting the majority of patients, whose prescription doses are low.

c) Among opioid prescription recipients in Washington state, **most opioid poisoning events did not occur at the time of having received an opioid prescription**.[30]

d) In Veterans Affairs data, overdose- and suicide-related events (including nonfatal events) were predicted by a wide range of factors that including mental diagnoses,

medical diagnoses, long-acting opioids, opioid dose, co-prescribed sedating substances and substance use disorder history.[31] In such models, a Veteran with post-traumatic stress disorder at low dose has higher risk than a similarly-aged veteran prescribed high dose. **Focusing on high-dose recipients would neglect the majority of persons with significant risk.**

e) In data from Kaiser Permanente of Colorado, **overdose risk was not predicted by prescribed dose at cohort inception**, but was predicted by a range of patient-specific variables, and the prescription of long-acting opioids.[32]

f) In data from Kaiser Permanente of Colorado, **variability in prescribed dose was associated with 3-fold elevation in overdose risk,** although patients who discontinued fully enjoyed lower overdose risk.[33]

g) In a safety-net clinic from Washington state, **prescription opioid stoppage was associated with a statistically significant three-fold elevation in risk of death** by overdose.[34]

h) In Veterans Affairs data, **opioid stoppage was associated with a large increase in the risk of death of the patient by both drug overdose and suicide**.[35] Increased overdose and suicide risk were also seen in the short term after **initiation** of opioid prescriptions. In combination these findings suggest instability in clinical care is a major driver of adverse outcomes.

i) In a San Francisco clinic, **prescription opioid stoppage was associated with transition to heroin use**.[36]

j) In Veterans Affairs data, large **reductions in overall opioid prescribing were not associated with reduction in rates of overdose death**, although they were associated with a smaller percentage of persons dying having received a prescription.[37]

Finally, we speak as witnesses concerned by what has happened to patients. To be sure, we have seen patients who tolerated opioid taper and perceived a benefit. And yet, the number of patients we have seen destabilized or harmed by prescription opioid taper or stoppage is shockingly high.

We acknowledge that it is difficult for health system leaders, clinicians and even journalists to understand how opioid stoppage or taper can be harmful. There are at least two possible accounts. First, opioids may still represent the only operational, effective treatment for assuring reasonable function among those with severe long-term pain, for some patients. Second, there is the matter of dependence when opioids are prescribed, which varies in how it manifests. Some opioid recipients show worsening emotional volatility and poor functioning on opioids, but nonetheless experience relief with each dose, and they do not meet criteria for an addiction diagnosis. In this situation, opioid taper often results in harm, including medical deterioration or suicidal ideation, even when taper is carried out slowly.[4]

In sum, the CDC Guideline's emphasis on dose as the primary point of leverage for patient safety was debatable in 2016, and that is still the case now. Of greater concern, however, is how it played out. Despite the merits of caution regarding dose escalation, the Guideline spurred actual mandates and mandates-in-effect to reduce dose across the board. And it did so even when patients were harmed. We regard this situation as an ethical breach. Our view is that

no patient should be treated as a means to an end. Each should be protected as an end in herself or himself.[38] That obligation has been misplaced. Section III will review this misapplication of the CDC's guidance.

III. The 2016 CDC Guideline did not adequately consider the context in which its authority would be invoked. A wide range of federal and non-federal agencies, including law enforcement and quality metric agencies, have enshrined the CDC's 90 MME threshold in ways that traumatize patients. Because this is taking place across many agencies, including US Department of Health and Human Services, the CDC must evaluate the use and misuse of its Guideline more robustly, and remediate through appropriate action.

Several private and public agencies, including authors of the CDC Guideline, have decried the misuse of the dose guidance statements presented within the CDC Guideline. Authors Dowell, Hagerich and Chou wrote in the New England Journal of Medicine that the Guideline did not seek to mandate forced reductions based on dose alone.[2] The Guideline itself declared prescribers "should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day"). As written, the 2016 Guideline did not require or insist on dose reduction for patients above such doses.

Unfortunately, cautionary statements about opioid dose were transformed into mandates and policy in quality metrics, in payer policies,[39] and taken up as investigative thresholds where the Department of Health and Human Services acts as a partner with law enforcement.[40] The CDC itself made efforts to avert such misapplication, three years after Guideline publication. The FDA has warned against rapid taper.[41] Sadly this public remonstration has proven ineffective, for the most part.

In particular, three quality agencies embraced the opioid dose metric of "percentage of patients receiving doses >90 MME" (earlier, 120 MME) as indicating poor care, which makes forced taper the default option for insurers and health care organizations. The agencies included the Pharmacy Quality Alliance, the National Quality Forum, and the National Committee for Quality Assurance. To be fair we also would have endorsed a view that a large clinical organization should see the number of patients at high dose as a sign of trouble, meriting focused quality improvement on whether shortfalls in pain care services have spurred dose escalation. Events, however, have proven our view somewhat naïve. None of the major quality metric agencies have declared an interest in reconsidering their dose metrics.

Similarly, other governmental and nongovernmental agencies have created an effective mandate to force doses down, without specific attention to pain care or patient safety. Among examples of official action, we'll note the current metric to allocate bonus payments under the Medicare Part D 5-Star program.[42] We also note the 2018 Congressional SUPPORT act requiring dose limits under Medicaid programs,[43] where – in some states- dose reduction is mandated for Medicaid patients.

Most concerning, in 2019, the HHS Office of the Inspector General published its view of the 2016 CDC Guideline as delineating 90 MME simply as the dose "to avoid" (without reference to the non-prohibitive nature of the Guideline, without reference to the CDC's account of "careful justification" for dose escalation, and without maintaining a distinction between forced dose reduction versus dose escalation).[40] In that report, the OIG declares using its analysis to support law enforcement investigations "through the Appalachian Regional Prescription Opioid Strike Force," a group including federal and non-federal law enforcement agencies. We are not privy to

the internal criteria used by law enforcement agencies in enforcement action. However, we find it concerning that a misreading of the CDC Guideline figures in HHS's published collaboration with law enforcement agencies.

It's important to understand that when legal authorities enter a practice to seize records for purpose of investigation, that step often effectively closes the practice and may terminate care for all patients, prior to any adjudication of the prescriber's guilt or innocence. In this regard, HHS-OIG appears to have published a collaboration with investigative agencies predicated on counting patients at >90 MME, with the effect of precipitating opioid stoppages that FDA itself warned against in 2019.

The overall situation has contributed to a documented reluctance of physicians to assume responsibility for patients who receive opioids.[44] It should be self-evident: where patients cannot obtain care at all, there is no possibility of protecting them.

Mitigation of harm to patients should be based on a salient recommendation received by the CDC in early 2016. At that time, the CDC's Opioid Guideline Workgroup urged that the CDC monitor for potential misapplication of its Guideline, which had not yet been adopted.[45] Should the CDC now choose to modify its Guideline, we urge a more robust system to evaluate how it is applied and to remediate harmful misapplication. The formal inclusion of patients and families as part of that system would greatly strengthen such efforts.

Conclusion:

At the present time, the CDC's efforts to address prescription opioid management, commendable as they are, have not been strongly anchored in accepted frameworks for the classification, assessment and care of persons with chronic pain. In 2016, that gap may well have been seen as an acceptable efficiency, given the prior role of opioid prescriptions in contributing to a crisis involving opioid use disorder and overdose. The Guideline's language attempted to prevent its own misapplication, declaring:

"The recommendations in the guideline are voluntary, rather than prescriptive standards. They are based on emerging evidence, including observational studies or randomized clinical trials with notable limitations. Clinicians should consider the circumstances and unique needs of each patient when providing care"

Four years later, we now understand that these cautionary statements were not successful. We believe that that the effort to guide opioid prescribing in isolation from a broader framework for pain care spurred misapplication of the Guideline, with patient harm as a result.

As experts committed to addressing twin crises in pain and in addiction care, we offer the strongest possible declaration of our willingness to assist the CDC in its deliberations going forward on this crucial matter.

Sincerely,

Stefan G. Kertesz, MD, MSc (skertesz@uabmc.edu)
Professor, University of Alabama at Birmingham School of Medicine and Birmingham VA Medical Center

Opioid Safety Initiative and Opiate Advice Team, Birmingham VA Medical Center
Implementation Team, Alabama Opioid Overdose and Addiction Council
Diplomate, American Board of Addiction Medicine

Ajay Manhapra, MD (ajay.manhapra@yale.edu)
Lead Physician, Advanced PACT Pain Clinic, Hampton VA Medical Center, Hampton, Virginia
Research Scientist, VA New England Mental Illness Research, Education and Clinical Center, West Haven, CT
Lecturer, Department of Psychiatry, Yale School of Medicine, New Haven, CT
Assistant Professor, Department of Physical Medicine and Rehabilitation and Psychiatry, Eastern Virginia Medical School, Norfolk, VA

Adam J. Gordon, MD MPH FACP DFASAM CMRO (adam.gordon@hsc.utah.edu)
Elbert F. and Marie Christensen Endowed Research Professorship
Professor of Medicine and Psychiatry, University of Utah School of Medicine
Chief, Addiction Medicine, Care, Salt Lake City VA Health Care System

References:

1. Raffaeli W, Arnaudo E. Pain as a disease: an overview. *J Pain Res.* 2017;10:2003-2008.
2. Dowell D, Haegerich T, Chou R. No Shortcuts to Safer Opioid Prescribing. *N Engl J Med.* 2019;380(24):2285-2287.
3. Manhapra A, Becker WC. Pain and Addiction: An Integrative Therapeutic Approach. *Med Clin North Am.* 2018;102(4):745-763.
4. Manhapra A, Arias AJ, Ballantyne JC. The conundrum of opioid tapering in long-term opioid therapy for chronic pain: A commentary. *Substance Abuse.* 2017:1-10.
5. The U.S. Department of Health and Human Services Working Group on Patient-Centered Reduction or Discontinuation of Long-term Opioid Analgesics. *HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. US Department of Health and Human Services. Accessed at https://www.hhs.gov/opioids/sites/default/files/2019-10/Dosage_Reduction_Discontinuation.pdf on June 16, 2020.* 2019.
6. Treede RD, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain.* 2019;160(1):19-27.
7. Nugraha B, Gutenbrunner C, Barke A, et al. The IASP classification of chronic pain for ICD-11: functioning properties of chronic pain. *Pain.* 2019;160(1):88-94.
8. Treede R-D, Rief W, Barke A, et al. A classification of chronic pain for ICD-11. *PAIN.* 2015;156(6):1003-1007.
9. Chou R, Hartung D, Turner J, et al. *Opioid Treatments for Chronic Pain. Comparative Effectiveness Review No. 229. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 20-EHC011. Rockville, MD: Agency for Healthcare Research and Quality; April 2020. DOI: https://doi.org/10.23970/AHRQEPCCER229.* 2020.
10. McDonagh MS, Selph SS, Buckley DI, et al. Nonopioid Pharmacologic Treatments for Chronic Pain. Comparative Effectiveness Review No. 228. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 20-EHC010. Rockville, MD: Agency for Healthcare Research and Quality; April 2020. DOI: https://doi.org/10.23970/AHRQEPCCER228. 2020.

11. Skelly AC, Chou R, Dettori JR, et al. *Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review Update. Comparative Effectiveness Review No. 227. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 20-EHC009. Rockville, MD: Agency for Healthcare Research and Quality; April 2020. DOI: https://doi.org/10.23970/AHRQEPCCER227.* 2020.
12. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2016;65(1):1-49.
13. Busse JW, Craigie S, Juurlink DN, et al. Guideline for opioid therapy and chronic noncancer pain. *Canadian Medical Association Journal.* 2017;189(18):E659-E666.
14. Opioid Therapy for Chronic Pain Work Group. *VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain. Accessed at https://www.healthquality.va.gov/guidelines/pain/cot/ on June 14, 2020.* Washington, DC: Department of Veterans Affairs and Department of Defense; March 1 2017.
15. Darnall BD, Juurlink D, Kerns RD, et al. International Stakeholder Community of Pain Experts and Leaders Call for an Urgent Action on Forced Opioid Tapering. *Pain Med.* 2018.
16. Kertesz SG, Gordon AJ. A crisis of opioids and the limits of prescription control: United States. *Addiction (Abingdon, England).* 2019;114(1):169-180.
17. Llorente E. *As doctors taper or end opioid prescriptions, many patients driven to despair, suicide. December 10, 2018. FoxNews. Accessed at https://www.foxnews.com/health/as-opioids-become-taboo-doctors-taper-down-or-abandon-pain-patients-driving-many-to-suicide on June 4, 2020.* December 10, 2018 2018.
18. Dahlhamer J, Lucas J, Zelaya C, et al. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults - United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2018;67(36):1001-1006.
19. Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth.* 2019;123(2):e273-e283.
20. Weiner SJ. *On becoming a healer : the journey from patient care to caring about your patients.* Baltimore: Johns Hopkins University Press; 2020.
21. Barry DT, Marshall BDL, Becker WC, et al. Duration of opioid prescriptions predicts incident nonmedical use of prescription opioids among U.S. veterans receiving medical care. *Drug Alcohol Depend.* 2018;191:348-354.
22. National Committee for Quality Assurance. *Proposed Changes to Existing Measure for HEDIS®1 2020: Use of Opioids at High Dosage (UOD).* Washington, D.C.: National Committee for Quality Assurance; February 12, 2019 2019.
23. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med.* 2010;152(2):85-92.
24. Bohnert ASB, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA.* 2011;305(13):1315-1321.
25. Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN. Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med.* 2011;171(7):686-691.
26. Bohnert AS, Logan JE, Ganoczy D, Dowell D. A Detailed Exploration Into the Association of Prescribed Opioid Dosage and Overdose Deaths Among Patients With Chronic Pain. *Med Care.* 2016;54(5):435-441.
27. Baumblatt JAG, Wiedeman C, Dunn JR, Schaffner W, Paulozzi LJ, Jones TF. High-Risk Use by Patients Prescribed Opioids for Pain and Its Role in Overdose Deaths. *JAMA Internal Medicine.* 2014;174(5):796-801.

28. Achenbach J, Bernstein L. *Opioid crackdown forces pain patients to taper off drugs they say they need. Washington Post. September 10, 2019. Accessed at https://www.washingtonpost.com/health/opioid-crackdown-forces-pain-patients-to-taper-off-drugs-they-say-they-need/2019/09/10/3920f220-c8da-11e9-a4f3-c081a126de70_story.html on June 14, 2020.* 2019.
29. Darke S. Heroin overdose. *Addiction (Abingdon, England).* 2016;111:2060-2063.
30. Fulton-Kehoe D, Sullivan MD, Turner JA, et al. Opioid poisonings in Washington State Medicaid: trends, dosing, and guidelines. *Med Care.* 2015;53(8):679-685.
31. Oliva EM, Bowe T, Tavakoli S, et al. Development and applications of the Veterans Health Administration's Stratification Tool for Opioid Risk Mitigation (STORM) to improve opioid safety and prevent overdose and suicide. *Psychological Services.* 2017;14(1):34-49.
32. Glanz JM, Narwaney KJ, Mueller SR, et al. Prediction Model for Two-Year Risk of Opioid Overdose Among Patients Prescribed Chronic Opioid Therapy. *Journal of general internal medicine.* 2018;33(10):1646-1653.
33. Glanz JM, Binswanger IA, Shetterly SM, Narwaney KJ, Xu S. Association Between Opioid Dose Variability and Opioid Overdose Among Adults Prescribed Long-term Opioid Therapy. *JAMA Netw Open.* 2019;2(4):e192613.
34. James JR, Scott JM, Klein JW, et al. Mortality After Discontinuation of Primary Care-Based Chronic Opioid Therapy for Pain: a Retrospective Cohort Study. *Journal of general internal medicine.* 2019;34(12):2749-2755.
35. Oliva EM, Bowe T, Manhapra A, et al. Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. *BMJ.* 2020;368:m283.
36. Coffin PO, Rowe C, Oman N, et al. Illicit opioid use following changes in opioids prescribed for chronic non-cancer pain. *PLoS One.* 2020;15(5):e0232538.
37. Lin LA, Peltzman T, McCarthy JF, Oliva EM, Trafton JA, Bohnert ASB. Changing Trends in Opioid Overdose Deaths and Prescription Opioid Receipt Among Veterans. *Am J Prev Med.* 2019;57(1):106-110.
38. Kant I, Ellington JW. *Grounding for the metaphysics of morals.* Indianapolis, Ind.: Hackett Pub. Co.; 1981.
39. Graig L, Olchefske I, Alper J. *Pain Management for People with Serious Illness in the Context of the Opioid Use Disorder Epidemic: Proceedings of a Workshop.* Washington, DC: National Academy of Sciences, Engineering and Medicine; 2019 2019.
40. United States Department of Health and Human Services Office of the Inspector General. *Concerns About Opioid Use in Medicare Part D in the Appalachian Region. Report OEI-02-18-00224. Accessed at https://oig.hhs.gov/oei/reports/oei-02-18-00224.pdf on June 10, 2020.* 2019.
41. United States Food and Drug Administration. *FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering.* Washington, DC April 9, 2019 2019.
42. Kaiser Family Foundation. *Issue Breif Reaching for the stars: quality ratings of Medicare Advantage plans, February 2011. [May 20, 2013]; Accessed at http://www.kff.org/medicare/upload/8151.pdf on June 10, 2020.*
43. United States Congress. Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act or the SUPPORT for Patients and Communities Act. In. *P.L. 115-271*2018.
44. Lagisetty PA, Healy N, Garpestad C, Jannausch M, Tipirneni R, Bohnert ASB. Access to Primary Care Clinics for Patients With Chronic Pain Receiving Opioids. *JAMA Netw Open.* 2019;2(7):e196928.

45. Opioid Guideline Workgroup. *Observations presented to the National Center for Injury Prevention and Control's Board of Scientific Counselors. January 28, 2016. Accessed at https://www.cdc.gov/injury/pdfs/bsc/bsc_summary.pdf on June 14, 2020.* Atlanta: Centers for Disease Control and Prevention.